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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/716,395

11/20/2000

Stephen W. Fesik

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EXAMINER

HARRIS, ALANA M

ART UNIT

PAPER NUMBER

1643

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/716,395	Applicant(s) FESIK ET AL.	
	Examiner Alana M. Harris, Ph.D.	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 10-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14 is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Arguments and Amendment

1. Claims 1-8 and 10-14 are pending.

Claim 1 has been amended.

Claims 1-8 and 10-14 are examined on the merits.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 1-8 and 10-13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicants' arguments and amendments to claim 1.

Maintained Grounds of Rejection

Claim Rejections - 35 USC § 112

4. The rejection of claims 1, 2, 4-8 and 10-13 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

Applicants suggest with the amendment of claim 1 the particular features of the mutant protein are known and the genus of the mutant proteins are finite and manageable, see Remarks submitted December 12, 2005, page 6. Applicants assert the description of the amino acids on the amino and carboxy termini surrounding the replacement sequence are clearly described in specification. Applicants aver one skilled in the art would know which acidic amino acids could be replaced within the flexible loop, see page 7 of the Remarks. In conclusion, Applicants note they "...have sufficiently described an adequate number of members of [the] ...claimed genus." These arguments and points of view have been fully considered, but found unpersuasive.

Applicants' amendment to claim 1 does not obviate the instant rejection because the pool has not been limited to evidence Applicants are in possession of all the mutant proteins claimed. While Applicants note the three wild-type Bcl-2 isoforms share all 239 amino acids except 3 residues this information does not limit the amount of changes that can still be made in the proteins and consequently yielding a huge pool of mutant proteins. It is understood that the replacement sequence comprises anywhere from 4 to about 50 amino acid residues comprising SEQ ID NO: 1 (16 amino acid residues). At the least two amino acids of the replacement sequence are replaced, meaning at most 48 additional amino acids can be changed as well.

Applicants attempt to establish a nexus between structure and function with the addition of the claim limitation, the mutant protein does not aggregate in solution does not aid in overcoming the instant rejection. As the claims are written the structure of the

claimed mutant proteins is not finite or resolute and it remains clear that Applicants have not sufficiently described an adequate number of members of the claimed genus.

There is no description of the amino acids residues on the amino terminus and carboxy terminus surrounding the replacement sequences. While the claims provide that the mutant protein must be *derived* from a wild-type human Bcl-2 protein, which does not provide adequate written description of the plethora of claimed mutant proteins.

Applicants are reminded “[t]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice...”, see 1242 OG 174, column 1, section 2, January 30, 2001. The claims continue to set forth a genus, which includes mutant proteins with substantial variation. “For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.”, see 1242 OG 174, column 1, section 2, January 30, 2001. For the reasons of record and set forth above the rejection is maintained.

5. The rejection of claims 1, 2, 4-8 and 10-13 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

Applicants note arguments directed to this rejection are of record in their arguments to the 35 U.S.C. 112, first paragraph, written description rejection and

respectfully request withdrawal, see Remarks, page 8, first full paragraph. Arguments and points of view have been carefully considered and have been found unpersuasive.

This rejection is maintained for the reasons of record and it remains that the specification provides insufficient evidence and guidance for making these mutant proteins and using these proteins the broadly claimed invention is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

Claim Rejections - 35 USC § 102

6. The rejection of claims 1-8 and 10-13 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,214,986 (filing date June 2, 1999) is maintained.

Applicants assert the Examiner has misinterpreted the patent and they have attempted to establish the differences between the proteins, see Remarks, page 9. Applicants assert the structures between the two proteins of interest are defined and well-known to those skilled in the art. Applicants also assert that amendments to claims should expedite prosecution. These points of view and arguments have been carefully considered, but found unpersuasive.

Applicants are reminded of what claim 1 requires. The claim requires a mutant protein, which is derived from wild-type human Bcl-2 proteins, SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 5. In essence, the claimed protein is not a wild-type human Bcl-2 protein. The mutant protein must have a replacement amino acid sequence comprising at least two acidic amino acids, which replaces a wild-type flexible loop comprising amino acid residues 35-91 of a wild-type human Bcl-2 protein. And lastly the mutant

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protein does not aggregate in solution. These requirements have been met by the prior art given the only structural requirement for the mutant protein is a replacement loop within amino acids 35-91 of a polypeptide with at least 239 amino acid residues derived from a wild-type human Bcl-2 protein. As the claims are written, particularly claim 1 the only required amino acids for the claimed mutant protein are at least two acidic amino acids within a 35-91 amino acids long protein.

Sequence 2 of patent '986 is regarded as the claimed human mutant protein because it contains a replacement amino acid sequence comprising at least two acidic amino acids instead of the wild-type's amino acid residues corresponding to a flexible loop. The replacement amino acid sequence comprises at least 16 amino acid residues of Applicants' SEQ ID NO: 1 as established in the attached listing of matches.

Sequence 2 is not SEQ ID NO: 3, 4 or 5 and can have amino acid sequences totally different from the wild-type sequences resulting in a changed, variant or mutant protein. And for these reasons the disclosed mutant protein reads on Applicants' broadly claimed mutant protein possessing all the properties of that claimed and the instant rejection is maintained.

7. The rejection of claims 1-8 and 10-13 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent number 5,646,008 (July 8, 1997) is maintained.

Applicants' arguments are essentially the same as presented above in the 102(e) rejection. These points of view have been carefully considered, but found unpersuasive.

Applicants are reminded of what claim 1 requires as stated in section 6.

Sequence 7 of patent '008 is regarded as the claimed human mutant protein because it contains a replacement amino acid sequence comprising at least two acidic amino acids instead of the wild-type's amino acid residues corresponding to a flexible loop. The replacement amino acid sequence comprises at least 16 amino acid residues of Applicants' SEQ ID NO: 1 as established in the attached listing of matches. Sequence 7 is not SEQ ID NO: 3, 4 or 5 and can have amino acid sequences totally different from the wild-type sequences resulting in a changed, variant or mutant protein. And for these reasons the disclosed mutant protein reads on Applicants' broadly claimed mutant protein possessing all the properties of that claimed and the instant rejection is maintained.

8. The rejection of claims 1-8 and 10-13 under 35 U.S.C. 102(b) as being anticipated by Boise et al. (Cell 74: 597-608, August 27, 1993/ IDS reference C3) is maintained.

Applicants' arguments are essentially the same as presented above in the previous 102 rejections. These points of view have been carefully considered, but found unpersuasive.

Figure 3 on page 599 of the article is regarded as the claimed human mutant protein because it contains a replacement amino acid sequence comprising at least two acidic amino acids instead of the wild-type's amino acid residues corresponding to a flexible loop. The replacement amino acid sequence comprises at least 16 amino acid

residues of Applicants' SEQ ID NO: 1 as established in the attached listing of matches. The amino acid sequence listed in Figure 3 is not SEQ ID NO: 3, 4 or 5 and can have amino acid sequences totally different from the wild-type sequences resulting in a changed, variant or mutant protein. And for these reasons the disclosed mutant protein reads on Applicants' broadly claimed mutant protein possessing all the properties of that claimed and the instant rejection is maintained.

9. The rejection of claims 1-8 and 10-13 under 35 U.S.C. 102(b) as being anticipated by Muchmore et al. (Nature 381:335-341, May 23, 1996/ IDS reference C7 is maintained.

Applicants' arguments are essentially the same as presented above in the previous 102 rejections. These points of view have been carefully considered, but found unpersuasive.

The first first listed sequence on page 337 is regarded as the claimed human mutant protein because it contains a replacement amino acid sequence comprising at least two acidic amino acids instead of the wild-type's amino acid residues corresponding to a flexible loop. The replacement amino acid sequence comprises at least 16 amino acid residues of Applicants' SEQ ID NO: 1 as established in the attached listing of matches. The first listed amino acid sequence listed in page 337 is also not SEQ ID NO: 3, 4 or 5 and can have amino acid sequences totally different from the wild-type sequences resulting in a changed, variant or mutant protein. And for these reasons the disclosed mutant protein reads on Applicants' broadly claimed mutant

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protein possessing all the properties of that claimed and the instant rejection is maintained.

10. Claim 14 is free of the art.

Allowable Subject Matter

11. Claim 14 is allowed.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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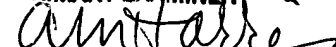
13. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours 7:30 am to 6:30 pm with alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.

PRIMARY EXAMINER



Alana M. Harris, Ph.D.

02 March 2006